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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/016,725	10/30/2001	Stephen M. Prouty	J&J-2065	4493

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EXAMINER	
RAO, MANJUNATH N	
ART UNIT	**PAPER NUMBER**
1652	

DATE MAILED: 06/03/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/016,725	PROUTY ET AL.	
	Examiner	Art Unit	
	Manjunath N. Rao, Ph.D.	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 March 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *7,9-13,25 and 27-39* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *7,9-13,25 and 27-39* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claims 7, 9-13, 25, 27-39 are currently pending and are present for examination.

Applicants' amendments and arguments filed on 3-8-04, have been fully considered and are deemed to be persuasive to overcome the rejections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 12-13, 30-31 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. Claims 12-13, 30-31 are drawn to a host cell comprising a nucleic acid which comprises a promoter sequence and an effector gene. The invention as claimed can be interpreted to read on a natural cell comprising said promoter along with its naturally associated with it. Therefore amending the claim to recite "a recombinant host cell" or "a host cell transformed with.." to show the hand of man would overcome this rejection.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 7, 9-13, 25, 27-39 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which

applicant regards as the invention. Claims 7 and 25 recite the phrase "effector gene". The metes and bounds of the above phrase is not clear to the Examiner. It is not clear to the Examiner as to whether the above phrase encompasses only heterologous polynucleotides encoding heterologous polypeptides (i.e., those polynucleotides not naturally linked to the above promoter) or the naturally linked to the above promoter sequence rendering the claim indefinite.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 7, 9-13, 25, 27-31 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the use of the polynucleotide comprising nucleotides 1 to about position 3958 or 3910 of SEQ ID NO:15 as a promoter sequence activating the transcription of a polynucleotide encoding a polypeptide, does not reasonably provide enablement for either making and using a variant of said polynucleotide comprising modification of 1-50 bases. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required, are summarized in In re Wands (858 F.2d 731, 8 USPQ 2nd 1400 (Fed. Cir. 1988)) as follows: (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the

prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claim(s).

Claims 7, 9-13, 25, 27-31 are so broad as to encompass making variants of nucleotides 1-3910 or 1-3958 of SEQ ID NO:15 and using such polynucleotides for promoter activity. The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the making of the variant polynucleotides and method of use of said polynucleotide or its variants for any purpose. It would require undue experimentation of the skilled artisan to make and use the claimed polynucleotides for the purposes of promoter activity. Since polynucleotides with a promoter activity have specific highly conserved and consensus sequences at specific positions, those skilled in the art would require the guidance and knowledge as to which specific nucleotide positions can be modified without affecting the promoter activity of the polynucleotide. Similarly, since polynucleotides can have a varied functional characteristics starting from encoding a polynucleotide to regulating or stabilizing transcription those skilled in the art would require guidance and knowledge as to which specific methods or processes are encompassed for use of the polynucleotide. Without such information those skilled in the art would not know how to make and how to use said polynucleotides. The specification is limited to teaching the use of polynucleotide (nucleotides 1 to 3910 or 3958 of SEQ ID NO:15) as a promoter but provides no guidance with regard to the making of variants and mutants or with regard to other uses. In view of the great breadth of the claim, amount of experimentation required to make the claimed polynucleotides, the lack of guidance, working examples, and unpredictability of the art in predicting function from a polynucleotide primary structure (e.g., see Ngo et al. in The Protein Folding Problem and Tertiary Structure Prediction,

1994, Merz et al. (ed.), Birkhauser, Boston, MA, pp. 433 and 492-495, Ref: U, Form-892), the claimed invention would require undue experimentation. As such, the specification fails to teach one of ordinary skill how to use the full scope of the polypeptides encompassed by this claim.

While recombinant and mutagenesis techniques are known, it is not routine in the art to screen for multiple substitutions or multiple modifications, as encompassed by the instant claims, and the positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the result of such modifications is unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions.

The specification does not support the broad scope of the claims which encompass all modifications and fragments of nucleotides 1 to 3910 or 3958 of SEQ ID NO:15 because the specification does not establish: (A) regions of the polynucleotide structure which may be modified without affecting promoter activity; (B) the general tolerance of said promoter to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any of the 1-50 nucleotide positions with an expectation of obtaining the desired biological function; (D)a rational and predictable scheme to use the claimed polynucleotide and its variants to specific purposes or processes; and (E) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims. The scope of the claims must bear a reasonable correlation with the scope of

enablement (*In re Fisher*, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, making the variant polynucleotides and determination of use of said polynucleotides is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

In response to the previous office action, applicants have traversed the above rejection arguing that mutagenesis techniques are known and the specification sets forth assays in which to test the resulting polynucleotides sequence for promoter activity and that there is no requirement that the variant have equivalent or even superior activity and therefore they assert that it would not be undue experimentation to make the variants. Examiner respectfully disagrees, because, while methods to produce variants of a known sequence such as site-specific mutagenesis, random mutagenesis, etc. are well known to the skilled artisan producing variants as claimed by applicants requires that one of ordinary skill in the art know or be provided with guidance for the selection of which specific nucleotide/s can be modified without affecting promoter activity. Without such guidance one of ordinary skill would be reduced to the necessity of producing and testing all of the virtually infinite possibilities. This would clearly constitute undue experimentation. While enablement is not precluded by the necessity for routine screening, if a large amount of screening is required, the specification must provide a reasonable amount of guidance with respect to the direction in which the experimentation should proceed. Such guidance has not been provided in the instant specification. Therefore the above rejection is maintained.

Claims 7, 9-13, 25, 27-39 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. These claims are directed to a genus of DNA molecules comprising steroyl-CoA desaturase gene as an effector gene that has not been described in the specification.

The specification does not contain any disclosure of the structure of all DNA sequences that are encompassed in the claims. The genus of DNAs that comprise these above DNA molecules is a large variable genus with the potentiality of having many different structures and also could read on the natural steroyl-CoA desaturase gene. Therefore, many structurally unrelated DNAs are encompassed within the scope of these claims, including partial DNA sequences. The specification discloses not even a single species of the claimed genus which is insufficient to put one of skill in the art in possession of the attributes and features of all species within the claimed genus. Therefore, one skilled in the art cannot reasonably conclude that the applicant had possession of the claimed invention at the time the instant application was filed.

Applicant is referred to the revised guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov.

In response to the previous rejection, applicants have traversed arguing that they have now provided the limitation of function "promoter activity" previously included in claims 8 and 26 now in claim 7 and 25 and therefore the rejection should be withdrawn. While Examiner has indeed withdrawn the previous rejection, he has instituted the new rejection because, applicants

have not limited the "effector gene" to only heterologous polynucleotides. Applicants are now claiming the full gene of human steroyl-CoA desaturase through the promoter without providing the structure. The above rejection can be withdrawn if applicants amend the claim by reciting "heterologous gene" in place of effector gene and cancellation of claims 10-11, 28-29 which are drawn to full length steroyl-CoA-desaturase.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claims 7, 9-13, 25, 27-39 are rejected under 35 U.S.C. 102(a) as being anticipated by Birren et al. (Database GenEmbl. Accession No. AC018783, 3-14-2000). This rejection is based upon the public availability of a polynucleotide sequence information in a public database. Claims 21-25, 30, 3-7, 12 of the instant application are drawn to an isolated polynucleotide comprising a nucleotide sequence from about nucleotide position 1 to about nucleotide position 3910 or 3958 or a variant thereof wherein said variant comprises deletions, additions, insertions and/or substitutions of from 1 to 50 bases of said sequences, vector and host cell comprising said polynucleotides. Birren et al. disclose a polynucleotide that is 159,351 bases long comprising the polynucleotide that is 99.3% identical to SEQ ID NO :15 comprising 2 deletions and 3 modified nucleotides linked to an effector gene. The reference also discloses vectors and host cells (clones) comprising said polynucleotide. The reference does not explicitly disclose that the

effector gene is that of a steroyl-CoA-desaturase gene. However, as the source of the instant polynucleotide and that of the reference are the same, examiner takes the position that such a characteristic is inherent to the reference polynucleotide and therefore anticipates above claims. Therefore, Birren et al. anticipate claims 7, 9-13, 25, 27-39 as written.

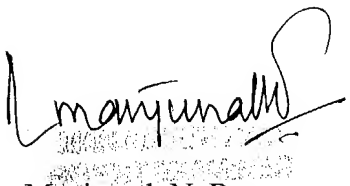
Since the Office does not have the facilities for examining and comparing applicants' polynucleotide with the polynucleotide of the prior art, the burden is on the applicant to show a novel or unobvious difference between the claimed product and the product of the prior art (i.e., that the protein of the prior art does not possess the same material structural and functional characteristics of the claimed protein). See *In re Best*, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and *In re Fitzgerald* et al., 205 USPQ 594.

In response to the previous Office action, applicants have traversed the above rejection arguing that they have now included the recitations of claims 8 and 26 into claims 7 and 25 and therefore the rejection must be withdrawn. Examiner respectfully disagrees. This is because as explained above, Birren et al. disclose a polynucleotide construct, that is 159,351 nucleotides in length, of which the promoter sequence comprises nucleotides 59,390 to 55,243. the reference nucleotide still has nearly 100,000 nucleotides downstream of the matched sequence which inherently reads on sequences of effector gene such as the steroyl-CoA-desaturase. Therefore, contrary to applicants argument, the reference continues to anticipate above claims. Therefore the above rejection is maintained.

Conclusion

None of the claims are allowable.

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Manjunath N. Rao, Ph.D. whose telephone number is 571-272-0939. The Examiner can normally be reached on 7.00 a.m. to 3.30 p.m. If attempts to reach the examiner by telephone are unsuccessful, the Examiner's supervisor, Ponnathapura Achutamurthy can be reached on 571-272-0928. The fax phone numbers for the organization where this application or proceeding is assigned is 703-872-9306 for regular communications and for After Final communications. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 571-272-1600.



Manjunath N. Rao
May 27, 2004